

Application No. 09/683,967  
Docket No. A1-1423  
Amendment dated December 30, 2003  
Reply to Office Action of November 7, 2003

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

Claim 1 (previously presented): A micromachined lysing device comprising:  
a substrate;  
a micromachined tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the substrate;  
a cell-containing fluid within the freestanding portion of the tube; and  
means for vibrating the freestanding portion of the tube at a level sufficient to rupture walls of cells in the fluid within the freestanding portion of the tube to produce a lysed material.

Claim 2 (original): A micromachined lysing device according to claim 1, wherein the vibrating means comprises:  
a first electrode associated with the freestanding portion of the tube;  
a second electrode associated with the substrate and facing the first electrode; and

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means for applying an electrostatic charge between the first and second electrodes.

Claim 3 (original): A micromachined lysing device according to claim 1, wherein the vibrating means comprises a piezoelectric element on a surface of the micromachined tube.

Claim 4 (original): A micromachined lysing device according to claim 1, further comprising a cap hermetically bonded to the substrate so as to define a hermetically-sealed enclosure containing at least the freestanding portion of the tube.

Claim 5 (currently amended): A micromachined lysing device according to claim 4, wherein the hermetically-sealed enclosure cavity is evacuated.

Claim 6 (original): A micromachined lysing device according to claim 1, wherein the substrate has a second surface oppositely disposed from the surface, the tube is disposed at the surface, and at least one of the fluid inlet and the fluid outlet is located at the second surface.

Claim 7 (previously presented): A micromachined lysing device according

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to claim 1, wherein the fluid contains a particulate matter for promoting rupturing of the walls of the cells.

Claim 8 (original): A micromachined lysing device according to claim 1, further comprising a raised surface feature on the substrate, the vibrating means being operable to impact the freestanding portion of the tube against the raised surface feature.

Claim 9 (original): A micromachined lysing device according to claim 1, wherein the vibrating means is operable to cause the freestanding portion of the tube to resonate.

Claim 10 (original): A micromachined lysing device according to claim 1, wherein the tube is a first tube of the micromachined lysing device, the micromachined lysing device further comprising a second tube having a freestanding portion, the second tube being in series with of the first tube.

Claim 11 (original): A micromachined lysing device according to claim 10, further comprising means for introducing a gel material into the lysed material after the lysed material leaves the freestanding portion of the first tube and before the lysed

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material enters the second freestanding portion of the second tube.

Claim 12 (original): A micromachined lysing device according to claim 11, further comprising means for vibrating the freestanding portion of the second tube at a level sufficient to mix the lysed material with the gel material.

Claim 13 (original): A micromachined lysing device according to claim 12, further comprising means for performing analysis on the lysed material after the lysed material leaves the freestanding portion of the second tube.

Claim 14 (original): A micromachined lysing device according to claim 13, wherein the first and second tubes and the analysis means are all supported on the substrate.

Claim 15 (original): A micromachined lysing device according to claim 1, wherein the substrate is formed of a semiconductor material and the tube comprises a micromachined portion of the substrate.

Claim 16 (original): A micromachined lysing device according to claim 1, wherein the tube comprises a micromachined semiconductor layer on the substrate.

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Claim 17 (original): A micromachined lysing device according to claim 1, further comprising means on the substrate for filtering cell wall fragments from the lysed material.

Claim 18 (original): A micromachined lysing device according to claim 1, further comprising means for delivering the fluid to the tube, the micromachined lysing device and the delivering means defining a handheld analysis unit.

Claim 19 (original): A micromachined lysing device comprising:  
a substrate formed of a semiconductor material;  
a micromachined tube formed of a semiconductor material, the tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the substrate;

a cap hermetically bonded to the substrate so as to define a hermetically-sealed enclosure containing at least the freestanding portion of the tube;

a cell-containing fluid flowing through the tube from the fluid inlet to the fluid outlet;

means for vibrating the freestanding portion of the tube at a level sufficient to rupture walls of the cells in the fluid as the fluid flows through the freestanding portion

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of the tube to produce a lysed material that leaves the tube through the fluid outlet;

means on the substrate for filtering cell wall fragments from the lysed material; and

means on the substrate for performing analysis on the lysed material after the lysed material is filtered.

**Claim 20 (original): A micromachined lysing device comprising:**  
a substrate;  
a micromachined tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the substrate;  
means for introducing a cell-containing fluid and a chemical lysing additive into the tube; and  
means for vibrating the freestanding portion of the tube at a level sufficient to mix the fluid and the chemical lysing additive to produce a lysed material that leaves the tube through the fluid outlet.

**Claim 21 (original): A micromachined lysing device according to claim 20, wherein the vibrating means comprises:**

a first electrode associated with the freestanding portion of the tube;

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a second electrode associated with the substrate and facing the first electrode; and

means for applying an electrostatic charge between the first and second electrodes.

Claim 22 (original): A micromachined lysing device according to claim 20, wherein the vibrating means comprises a piezoelectric element on a surface of the micromachined tube.

Claim 23 (canceled)

Claim 24 (currently amended): A micromachined lysing device according to claim 20, claim 23; wherein the hermetically-sealed enclosure cavity is evacuated.

Claim 25 (original): A micromachined lysing device according to claim 20, further comprising means for performing analysis on the lysed material.

Claim 26 (original): A micromachined lysing device according to claim 25, further comprising means for filtering cell wall fragments from the lysed material.

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Claim 27 (original): A micromachined lysing device according to claim 26, wherein the tube, the filtering means, and the analysis means are all supported on the substrate.

Claim 28 (original): A micromachined lysing device according to claim 20, wherein the substrate is formed of a semiconductor material and the tube comprises a micromachined portion of the substrate.

Claim 29 (original): A micromachined lysing device according to claim 20, wherein the tube comprises a micromachined semiconductor layer on the substrate.

Claim 30 (original): A micromachined lysing device according to claim 20, further comprising means for delivering the fluid to the tube, the micromachined lysing device and the delivering means defining a handheld analysis unit.

Claim 31 (original): A micromachined lysing device comprising:  
a substrate formed of a semiconductor material;  
a micromachined tube formed of a semiconductor material, the tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the

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substrate;

a cap hermetically bonded to the substrate so as to define a hermetically-sealed enclosure containing at least the freestanding portion of the tube;

a cell-containing fluid and a chemical lysing additive flowing through the tube from the fluid inlet to the fluid outlet;

means for introducing the fluid and the chemical lysing additive into the tube;

means for vibrating the freestanding portion of the tube at a level sufficient to mix the fluid and the chemical lysing additive as the fluid flows through the freestanding portion of the tube to produce a lysed material that leaves the tube through the fluid outlet;

means on the substrate for filtering cell wall fragments from the lysed material; and

means on the substrate for performing analysis on the lysed material after the lysed material is filtered.

Claim 32 (original): A method of lysing a cell-containing fluid, the method comprising the steps of:

flowing the fluid through a micromachined tube on a substrate, the tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the

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substrate; and

vibrating the freestanding portion of the tube at a level sufficient to rupture walls of the cells in the fluid as the fluid flows through the freestanding portion of the tube to produce a lysed material that leaves the tube through the fluid outlet.

Claim 33 (original): A method according to claim 32, wherein the vibrating step is performed by applying an electrostatic charge between the tube and the substrate.

Claim 34 (original): A method according to claim 32, wherein the vibrating step is performed with a piezoelectric element on a surface of the micromachined tube.

Claim 35 (original): A method according to claim 32, further comprising the step of introducing a particulate matter into the fluid prior to the fluid entering the freestanding portion of the tube, the particulate matter being introduced in an amount sufficient to promote rupturing of the walls of the cells.

Claim 36 (original): A method according to claim 32, wherein the freestanding portion of the tube impacts a portion of the substrate during the vibrating step.

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Claim 37 (original): A method according to claim 32, wherein the vibrating step causes the freestanding portion of the tube to resonate.

Claim 38 (original): A method according to claim 32, further comprising the step of flowing the lysed material through a second tube having a freestanding portion.

Claim 39 (original): A method according to claim 38, further comprising the step of introducing a gel material into the lysed material before the lysed material enters the second tube.

Claim 40 (original): A method according to claim 39, further comprising the step of vibrating the freestanding portion of the second tube at a level sufficient to mix the lysed material with the gel material.

Claim 41 (original): A method according to claim 40, further comprising the step of performing analysis on the lysed material after the lysed material leaves the freestanding portion of the second tube.

Claim 42 (original): A method according to claim 41, further comprising the step of filtering cell wall fragments from the lysed material.

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Claim 43 (original): A method according to claim 42, wherein the filtering step and the analysis step are performed on the substrate.

Claim 44 (original): A method of lysing a cell-containing fluid, the method comprising the steps of:

flowing the fluid through a micromachined tube formed of a semiconductor material and supported by a substrate formed of a semiconductor material, the tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the substrate and hermetically sealed within an evacuated enclosure defined by a cap bonded to the substrate;

vibrating the freestanding portion of the tube at a level sufficient to rupture walls of the cells in the fluid as the fluid flows through the freestanding portion of the tube to produce a lysed material that leaves the tube through the fluid outlet;

filtering cell wall fragments from the lysed material; and then performing analysis on the lysed material; wherein the filtering step and the analysis step are performed on the substrate.

Claim 45 (original): A method of lysing a cell-containing fluid, the method

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comprising the steps of:

flowing the fluid and a chemical lysing additive through a micromachined tube on a substrate, the tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the substrate; and

vibrating the freestanding portion of the tube at a level sufficient to mix the fluid and the chemical lysing additive as the fluid and the chemical lysing additive flow through the freestanding portion of the tube to produce a lysed material that leaves the tube through the fluid outlet.

Claim 46 (original): A method according to claim 45, the vibrating step is performed by applying an electrostatic charge between the tube and the substrate.

Claim 47 (original): A method according to claim 45, wherein the vibrating step is performed with a piezoelectric element on a surface of the micromachined tube.

Claim 48 (original): A method according to claim 45, wherein the vibrating step is performed within a hermetically-sealed enclosure containing at least the freestanding portion of the tube.

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Claim 49 (original): A method according to claim 48, wherein the hermetically-sealed cavity is evacuated.

Claim 50 (original): A method according to claim 45, further comprising the step of performing analysis on the lysed material.

Claim 51 (original): A method according to claim 50, further comprising the step of filtering cell wall fragments from the lysed material before performing the analysis.

Claim 52 (original): A method according to claim 51, wherein the filtering step and the analysis step are performed on the substrate.

Claim 53 (original): A method of lysing a cell-containing fluid, the method comprising the steps of:

flowing the fluid and a chemical lysing additive through a micromachined tube formed of a semiconductor material and supported by a substrate formed of a semiconductor material, the tube comprising a fluid inlet, a fluid outlet, and a freestanding portion between the fluid inlet and the fluid outlet, the freestanding portion being spaced apart from a surface of the substrate and hermetically sealed within an

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evacuated enclosure defined by a cap bonded to the substrate;  
vibrating the freestanding portion of the tube at a level sufficient to mix the fluid and the chemical lysing additive as the fluid and the chemical lysing additive flow through the freestanding portion of the tube to produce a lysed material that leaves the tube through the fluid outlet;  
filtering cell wall fragments from the lysed material; and then performing analysis on the lysed material;  
wherein the filtering step and the analysis step are performed on the substrate.